Community-acquired *Escherichia coli* meningitis in adult

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Abstract

We report a case of E. coli *meningitis presented initially without nuchal rigidity. Despite intensive care treatment, CSF was not sterilized and the patient died at 17 days after his admission. Patients with an unexplained altered sensorium with fever should undergo LP to evaluate for this rare entity and to direct early antimicrobial treatment which possesses efficacy for meningeal infection.*

Introduction

The overall annual attack rate for bacterial meningitis defined by a surveillance study in the US from 1978 through 1981, was approximately 3.0 cases per 100,000 populations[1]. The three most common meningeal pathogens, *Streptococcus pneumonia* (47%), *Neisseria meningitides* (25%), group B streptococcus (12%), accounted for more than 80% of such cases[2]. Durand et al attributed 17% of all cases of bacterial meningitis in a mainland United States hospital to Gram negative bacilli[3]. Common organisms in this group include *Klebsiella* species, *Pseudomonas* species, *Acinetobacter* species and *Enterobacter* species. *E. coli* accounted for only 6 % of all cases of meningitis due to Gram negative bacilli and thus represented about 1% of all cases of bacterial meningitis in adult. Therefore, we report a case report of *E. coli* meningitis and focus on the etiology with literature reviews.

Case report

History and physical examination at presentation

A 71 year-old Filipino male with a past medical history significant for alcohol abuse, gout and hypertension was admitted with a chief complaint of abdominal pain. He was in his usual state of health until 5 days prior to admission when he developed mild generalized abdominal pain associated with nausea and chills. Three days prior to admission he sought medical attention and the patient was begun on an oral first-generation cephalosporin for a presumptive diagnosis of urinary tract infection.

Two days prior to admission he noted a mild headache accompanied by worsening of the abdominal pain and vomiting. The history was negative for head trauma, upper respiratory infection, sinusitis, diarrhea, skin rash, diabetes mellitus, illegal drug use, or any sick contact. The patient was an immigrant from the Philippines in 1970 and a retired sugar cane farmer. The timing of his last visit to the Philippines was unknown.

On arrival at the Emergency Department, the patient was lethargic and exhibited generalized weakness, malnourishment and respiratory distress. His systolic blood pressure was 80 mmHg, heart rate 144 beats/min (regular rhythm), respiration rate 50/min, temperature 103.9 degrees Fahrenheit and oxygen saturation of 96% on inspired room air. Pupillary reflexes were sluggish bilaterally. Abdominal examination revealed generalized tenderness with guarding and rebound with diminished bowel sounds. A stool guaiac test was negative. There was no evidence of nuchal rigidity or focal neurological deficits.

Initial lab data

White blood cell (WBC) 11,700 /L, 48 % bands (no eosinophils), hemoglobin 12.5 g/dL, platelet count 56,000 /L, sodium 134 mmol/L, potassium 2.9 mmol/L, chrolide 93 mmol/L, CO_2 24 mmol/L, anion gap 17, BUN 15 mg/dL, creatinine 1.4 mg/dL. Total protein 5.2 g/dL, albumin 1.6 g/dL, mild elevation of AST and ALT, and normal amylase and NH_3. Arterial blood gas on room air showed PH 7.52, $PaCO_2$ 23.2mmHg, PaO_2 72.3 mmHg, O2 saturation 94.4 %, Base deficit -2.6, and HCO3 18.6 mmol/L. The admission chest film was unremarkable and the urinalysis revealed many bacteria and was positive for nitrates.

Subsequent hospital course

The patient was initially fluid resuscitated successfully in the emergency department. However his level of consciousness gradually deteriorated although during this time period the patient never complained of neck pain or stiffness.

Two hours after arriving at the ED, piperacillin/tazobactam 3.375g was administered once intravenously because of the suspicion of peritonitis. Abdominal imaging included a right upper quadrant ultrasound and abdominal/pelvic CT scan, which revealed mild

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ascites and gall bladder wall thickening without evidence of gall bladder stones or dilated bile ducts.

A surgical consultation was obtained, however exploratory laparotomy was not performed due to some improvement in the abdominal signs. However, during the next few hours the patient exhibited progressive deterioration of mental status and a new right hemiparesis. On repeat exam, the patient was comatose but his neck was supple. Several hours later, when the patient was transferred to the intensive care unit, nuchal rigidity was detected on examination.The patient was subsequently intubated for protection of his airway, then a lumbar puncture (LP) was immediately performed. The cerebrospinal fluid (CSF) was purulent with an elevated opening pressure of 43.5 cm H_2O. CSF cell count showed WBC 1,670 /ul (polymorphonuclear cell 85 %), CSF glucose <2 mg/dL (serum glucose 116 mg/dL), and a CSF protein of 395 mg/dl. Initially ceftriaxone 2g every 12 hour and ampicillin/sulbactam 3g every q 6 hour were administered intravenously. After the CSF Gram s stain demonstrated gram-negative bacilli, antimicrobial agents were changed to ceftazidime 2g every 8 hour and gentamycin 80mg every 8 hour intravenously to cover *P.aeruginosa*. On day 3, after the susceptibility test to *E.coli* of CSF was obtained, antimicrobial agents were changed to ceftriaxone 2g every 12 hour, and then ceftriaxone monotherapy was continued until day 17.

On day 2, a brain MRI showed acute infarction involving the left thalamus, left gangliocapsular region and left corona radiata. The T-2 flair images demonstrated a diffusely abnormal signal along the leptomeningeal surfaces, consistent with meningitis. Cultures of CSF, blood and urine grew *E. coli* sensitive to ceftriaxone but resistant to ampicillin and bactrim. Initial Blood culture, urine and CSF culture were the same sensitivity profile. The following were the minimum inhibitory concentration of *E. coli* susceptibility in CSF culture (ampicillin ≥32 microgram per mL, ceftazidime 8 microgram per mL, ceftriaxone ≤8 microgram per mL, gentamicin ≤1 microgram per mL, trimethoprim/sufamethoxazole ≥320 microgram per mL). Sputum culture on admission and stool ova & parasite on day 6 were negative. On day 2, blood culture was negative.

On day 10, a follow-up CSF culture remained positive for *E. coli* with no change in sensitivity (exactly the same MIC as the previous CSF culture), and WBC increased from 1,670 /ul to 2,275 /ul. During his 2 weeks hospitalization, he remained in the comatose state and continued to deteriorate. His leukocyte count continued to increase up to 20,000/mm. On day 17, the patient was withdrawn from life support by his family member due to persistent comatose and expired despite continuation of appropriate antibiotic treatment. Necropsy was refused by his family.

Discussion

Risk and prognostic factors

Bacterial meningitis due to Gram negative bacilli can be broadly classified according to the portal of entry of the organisms into the CSF. The most frequent cause in adults is dura-arachinoid disruption following neurosurgery or trauma[4]. Less frequently, spontaneous infection occurs without disruption of the blood-brain barrier. Non-traumatic meningitis due to Gram negative bacilli is rarely community-acquired, but can occasionally occur in patients who are immunosuppressed from conditions such as diabetes mellitus, alcoholism and chronic liver disease or malignant disease[4]. Of all non-traumatic meningitis due to Gram negative bacilli seen at the Detroit Medical Center, 60 % of patients with *E. coli* meningitis were chronic alcoholics and 67 % of cases were diagnosed concomitantly with urinary tract infection[5].

Microbiologically, our patient had the same sensitivity profile among CSF, blood culture and urine culture. The best explanation is that the patient had *E. coli* bacteremia from the urinary tract infection and *E. coli* was seeded in CSF. Another possibility was that liver cirrhosis or some undetected intraabdominal source especially from gastrointestinal tract might cause *E. coli* bacteremia, then *E. coli* was transferred to CSF. This patient might have had occult spontaneous bacterial peritonitis as a cause of his abdominal pain, although a paracentesis was not conducted.

A study in Thailand reported 85 patients with community-acquired bacterial meningitis in adults[6]. *E. coli* meningitis was the second most common organism (14%) and the incidence increased in patients older than 45 years. *E. coli* meningitis was associated with steroid intake 25% (3/12), strongyloidiasis 25% (3/12) and history of head injury 17% (2/12).

E. coli meningitis has been described in Strongyloidiasis[7] with special mention of cases due to *Escherichia coli* with hyperinfestation leading to auto-infection and either hematogenous spread of *E. coli* contaminated filariaform larva which disseminate to the central nervous system or pure *E. coli* bacteremia. *E. coli* meningitis secondary to pulmonary Strongyloidiasis in an immunocompromised patient was also reported[8]. Our patient was an immigrant from the Philippines, a tropical geography endemic for *S. stercoralis* infection, and probably immunosuppressed to some extent due to alcoholism and debilitated body habitus. However in our case, the lack of recent steroid therapy and the lack of stool parasites make disseminated Strongyloidiasis unlikely.

The virulence of the *E. coli* strain may also be an important factor. In a recent study by Kim et al, *E. coli* serotype K1 would only successfully traverse the blood brain barrier if there was a high degree of bacteremia and invasion of brain microvascular endothelial cells[9]. In Kim s study, adult animals required 10^6-fold-greater inoculum of *E.coli* K1 to induce a similar high-level bacteremia than neonatal animals. This suggested that the age dependency of *E.coli* meningitis was due to the relative resistance of adults to high-level bacteremia, which preceded the development of meningitis, and less likely due to greater invasion of neonatal brain microvascular endothelial cells (BMEC) compared to adults BMEC. *E.coli* meningitis is commonly associated with neonatal meningitis. These data partly explains that *E.coli* is commonly associated with neonatal meningitis.

Bacterial meningitis continues to have a high mortality, yet it remains a treatable disease especially with the availability of potent antibiotic therapy. To maximize a favorable recovery, rapid initiation of appropriate antibiotics is crucial. However, at times, bacterial meningitis may be difficult to diagnose due to atypical presentations, such as was the case here where the dominant early symptom was abdominal pain.

Interestingly our patient had multiple risk factors for *E. coli* meningitis; a history of alcoholism and an active urinary tract infection, in addition to *E. coli* bacteremia. Thus, the pathogenesis of *E. coli* meningitis may have occurred by several possible pathways.

The mortality rate in spontaneous meningitis due to Gram nega-

tive bacilli varies from 50-75%[5,10,11]. A study of community-acquired meningitis showed that the overall mortality was 34% and the mortality for patients with *E. coli* meningitis was 41.6%[6]. Prognostic factors of Gram negative bacillary meningitis have been reported by Lu et al[12]. Septic shock, initial conscious level, initial appropriate antibiotic treatment, the presence of hyperosmolar hyperglycemic nonketotic coma, disseminated intravascular coagulopathy (DIC), CSF WBC count (≥ 1000 cell/mm^3), low CSF glucose concentration (< 50mg/dL), and CSF lactate concentration (≥ 90 mg/dL) were statistically significant prognostic factors. Our case had several these factors, such as DIC, persistent CSF WBC count (≥ 1000 cell/mm^3), and low CSF glucose concentration.

Among these factors, only inappropriate antimicrobial therapy and septic shock were strongly associated with mortality rate after adjusting for confounding factors[12]. Appropriate immediate antimicrobial treatment at adequate doses for meningeal infection is an unqualified "standard of care" for patients with suspected bacterial meningitis. Adverse clinical outcome has been associated with a delay in initiation of antibiotic therapy[13].

Our patient presented with a significantly altered mental status, and was given piperacillin/tazobactam immediately for a suspected acute abdomen. Inappropriate antibiotic administration may have been a prognostic factor in this case. Piperacillin/tazobactam is not recommended as an empiric antibiotic for meningitis; additionally the dose which the patient had was insufficient for bacterial meningitis. An appropriate antibiotic for meningitis, ceftriaxone, was given about 10 hours after his arrival at the ED. The delay of appropriate antibiotic administration was due to the atypical presentation of *E. coli* bacterial meningitis. Intrathecal or intraventricular aminoglycosides are rarely needed in current practice. The added benefits of intrathecal or intraventricular aminoglycosides for such infection is suggested in the literature but not established by randomized controlled trials[14] with special mention of cases due to *Escherichia coli*.

Conclusion

E.coli is a rare cause of community-acquired meningitis and may present in an atypical fashion with abdominal symptoms and signs, and a lack of meningeal signs. Hematogenous dissemination is the most likely pathway to the central nervous system. Patients with an unexplained altered sensorium and an abdominal presentation should undergo LP to evaluate for this rare entity and to direct early antimicrobial treatment which possesses efficacy for meningeal infection. Despite appropriate antimicrobial therapy the outcome may be poor due to the virulence of this organism and underlying compromise of the host defenses.

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